contributing; we are pushing our own minds and the minds of others. In the very best world possible, this is why we went into medicine and into the trying world of oncology.

Sitting in a dark room with the comforting glow of the overhead projector, I listen as an expert describes a signaling cascade, a new drug, the findings of a recent clinical trial. As she lectures, these same pathways and molecules exist in her own body. This expert could harbor deadly mutations and dysregulated proteins. I am struck by this paradox. In trying to solve the mysteries of our own bodies, the bodies of our loved ones, and the bodies of people we do not even know yet, we find ourselves leveled and completely vulnerable.

I stand next to my poster with my own small contribution on display. I am amazed that people are interested in what I have to say; some even take notes. I am an authority on this one concept and it is intoxicating. My family and friends are proud. They ask, "So you stand in front of a poster and do what?" They wait to hear how it went and to tell me about all of the news clips coming out of Orlando. There are cheerleaders behind everyone; from the plenary speakers with the big names to those with names just as big in their own families and communities.

When it is over, I am energized and exhausted at the same time. The knowledge and advice I have gained are like small parcels that I pack away with me in my suitcase. I drive by the convention center in a taxi and see people finishing up a last session, talking on cell phones to family, exchanging business cards with colleagues. I leave the insulated fold of so much concentrated intelligence and purpose, and return to the real world. But I look forward to returning, every year that I can, for a dose of inspiration, education, and perspective.

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Cutaneous Lymphomas Reported to the National Cancer Institute's Surveillance, Epidemiology, and End Results Program: Applying the New WHO–European Organisation for Research and Treatment of Cancer Classification System

To the Editor: As noted in the recent study by Smith et al,[1] there is a paucity of data describing primary cutaneous B-cell lymphoma in the United States, and discordant results have been reported in other countries. Interestingly, the study by Smith et al[1] was published nearly synchronously with the new WHO–European Organisation for Research and Treatment of Cancer (EORTC) classification system for primary cutaneous lymphoma, which utilized data from the Dutch and Austrian Cutaneous Lymphoma Group (DACLG) to describe the relative frequency and survival of the entities within the new classification.[2] Using the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program, we sought to apply the WHO-EORTC classification system to compare results with results from the DACLG.

The SEER program classifies information on histology and topography according to the *International Classification of Diseases for Oncology–Third Edition* (ICD-O-3).[3] Using ICD-O codes specified in the WHO Classification of Tumors of Hematopoietic and Lymphoid Tissues and histologic descriptions of the WHO-EORTC classification, we attempted to categorize primary cutaneous lymphomas (histology codes 9670-9729 and topography codes C440-C449) in SEER into categories specified in the WHO-EORTC system (see Appendix).[2,4] In those instances where entities in the WHO-EORTC system were not specified in the ICD-O-3 coding scheme, we included the entities under broader disease categories. Incidence rates (IR) and disease-specific 5-year actuarial survival were derived from SEER*Stat 6.1.4.[5]

We identified 4,310 cases of primary cutaneous lymphoma diagnosed from 1992 to 2002 among patients in 13 population-based cancer registries. Primary cutaneous T-cell lymphoma and primary cutaneous B-cell lymphoma accounted for 76.9% and 22.7% of cases in SEER, respectively (Table 1), similar to the DACLG.[2] Mycosis fungoides was the most common entity in SEER (45%; IR = 0.51 per 100,000 person-years) and in the DACLG (44%). Sézary syndrome was relatively rare in SEER (1.3%; IR = 0.02) and in the DACLG (3%). Taken together, entities comprising the broader category of peripheral T-cell lymphoma made up more than 25% (IR = 0.29) of cutaneous lymphomas in SEER compared with less than 6% in the DACLG. Collectively, diffuse large B-cell lymphoma comprised 12% (IR = 0.14) of the cutaneous lymphomas in SEER, and was associated with a disease-specific 5-year survival of 81.7%. In comparison, diffuse large B-cell lymphoma accounted for less than 6% of all cutaneous lymphomas in the DACLG, and had a disease-specific 5-year survival of 50% to 65%.

In sum, when categorizing primary cutaneous lymphoma according to the new WHO-EORTC classification system, similarities and differences were noted between SEER and the DACLG. We did not undertake a centralized clinical and pathologic review of cases, but rather relied on ICD-O codes that reflect the diagnostic practices of clinicians across the 13 registry catchment areas in the United States. As the WHO-EORTC classification for cutaneous

Table 1. Incidence Rates and 5-Year Disease-Specific Actuarial Survival of 4,310 Patients With Primary Cutaneous Non-Hodgkin's Lymphoma Diagnosed in SEER-13, 1992-2002

	No. of Cases	%	IR*	Disease-Specific 5-Year Survival (%)†
Cutaneous non-Hodgkin lymphoma, all‡	4,310	100.0	1.14	86.9
Primary cutaneous T-cell lymphoma, all	3,316	76.9	0.87	87.0
Indolent clinical behavior				
Mycosis fungoides	1,941	45.0	0.51	91.5
CD30+ lymphoproliferative disorders	202	4.7	0.05	83.4
Subcutaneous panniculitis-like T-cell lymphoma	10	0.2	—§	—§
Aggressive clinical behavior				
Sézary syndrome	55	1.3	0.02	41.7
NK/T-cell lymphoma, nasal type	10	0.2	—§	—§
Combined (indolent and aggressive behavior)				
Peripheral T-cell lymphoma	1,098	25.5	0.29	83.2
Primary cutaneous B-cell lymphoma, all	980	22.7	0.26	86.7
Indolent clinical behavior				
Marginal zone B-cell lymphoma	232	5.4	0.06	95.1
Follicle center lymphoma	219	5.1	0.06	90.6
Intermediate clinical behavior				
Diffuse large B-cell lymphoma, all	517	12.0	0.14	81.7
Leg	89	2.1	0.02	64.5
Specified site, other than leg	365	8.5	0.10	85.4
Overlapping lesions or unspecified site	63	1.5	0.02	78.7

Abbreviations: SEER, Surveillance, Epidemiology, and End Results; IR, incidence rate; NK, natural killer; WHO-EORTC, World Health Organization–European Organisation for Research and Treatment of Cancer.
*Incidence rates are expressed per 100,000 person-years, age-adjusted to the 2000 United States population.
†Individuals with unknown cause of death were censored.
‡Includes mantle cell lymphoma (n = 8), Burkitt's lymphoma (n = 4), and precursor cell lymphoblastic lymphoma (n = 14) not specified in the WHO-EORTC classification system.
§Fewer than 16 incident cases.

lymphoma is incorporated into the community, diagnostic practices will evolve to reflect the new classification system. By necessity, the ICD-O coding scheme will similarly need to incorporate the new entities defined in the WHO-EORTC classification. Our discordant results suggest that we were currently unable to completely translate SEER data into WHO-EORTC categories. The extent to which geographic variation between United States and European populations, diagnostic misclassification, treatment, or other factors contribute to our findings is uncertain. Large-scale population-based data can be used to complement information from smaller clinical studies to advance our understanding of lymphomas. However, to maximize the potential of population-based data for primary cutaneous lymphoma, classification schemes will need to evolve in parallel.

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Appendix

ICD-O-3 codes corresponding to cutaneous lymphoma subtypes included in Table 1: Mycosis fungoides [9700]. ICD-O codes for WHO–European Organisation for Research and Treatment of Cancer (EORTC) – defined mycosis fungoides subtypes and variants (folliculotropic mycosis fungoides, pagetoid reticulosis, granulomatous slack skin) were not available. CD30+ lymphoproliferative disorders [9714, 9718] included anaplastic large cell lymphoma (T-cell and null-cell type) and primary cutaneous CD30+ T-cell lymphoproliferative disorder, including lymphomatoid papulosis. WHO-EORTC entities included herein are primary cutaneous anaplastic large cell lymphoma and lymphomatoid papulosis. Subcutaneous panniculitis-like T-cell lymphoma [9708]. Sézary syndrome [9701]. NK/T-cell lymphoma, nasal type [9719]. Peripheral T-cell lymphoma [9702, 9705, 9709] included mature T-cell lymphoma, not otherwise specified; angioimmunoblastic T-cell lymphoma; and cutaneous T-cell lymphoma, not otherwise specified. WHO-EORTC entities included herein include CD4+ small/medium pleomorphic T-cell lymphoma (indolent clinical behavior) and aggressive CD8+ T-cell lymphoma, γ/δ T-cell lymphoma, and peripheral T-cell lymphoma (all with aggressive clinical behavior). Marginal zone B-cell lymphoma [9670, 9671, 9699] included malignant lymphoma, small B lymphocytic, not otherwise specified; malignant lymphoma, lymphoplasmacytic; and marginal zone B-cell lymphoma, not otherwise specified. Follicle center lymphoma [9690, 9691, 9695, 9698] included follicular lymphoma, not otherwise specified; follicular lymphoma, grade 2; follicular lymphoma,

grade 1; and follicular lymphoma, grade 3. Diffuse large B-cell lymphoma [9675, 9680, 9684] included malignant lymphoma, mixed small and large cell, diffuse; malignant lymphoma, large B-cell, diffuse, not otherwise specified; and malignant lymphoma, large B-cell, diffuse, immunoblastic, not otherwise specified. ICD-O-3 topography codes: leg [C447], specified site other than leg [C440-446], overlapping lesions or unspecified site [448-449].

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The authors indicated no potential conflicts of interest.

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Heparin and CXCL12 Dimerization

To the Editor: We read with great interest the article by Lee et al[1] that investigated the influence of a low-molecular-weight heparin dalteparin on the survival of patients with active cancer and acute venous thromboembolism. They found that the use of dalteparin relative to coumarin derivatives was associated with improved survival in patients with solid tumors who did not have metastatic disease at the time of an acute venous thromboembolic event. Currently, the mechanisms for a potential antineoplastic effect of low-molecular-weight heparins remain unknown. As the authors implied in the article, one possibility might be the antiangiogenic effects of this drug. We want to propose a different mechanism of its action that may lead to increased survival, especially in patients who do not have metastatic disease. Chemokines and their respective receptors' expression have recently been demonstrated in the development of primary tumors and metastases.[2] In particular, chemokine receptors CXR4 and CCR7 are highly expressed in malignant breast tumors and metastases. Their respective ligands, stromal cell-derived factor-1 (CXCL12/SDF-1) and CCL21/6Ckine, are expressed in organs that represent important sites of breast cancer metastasis, such as bone marrow, liver, and lung.[3] This mechanism has also been implicated in other cancers. Although it is not known whether the monomeric or dimeric structure of CXCL12 is responsible for signaling in vivo, a recent study found that acidic pH promotes the monomeric state of CXCL12 by destabilizing the dimeric structure, while heparin binding promotes CXCL12 dimer formation.[4] Given the information above, we propose that heparin might prevent invasive and metastatic capacity of cancer cells by shifting CXCL12 monomer-dimer equilibrium to a dimerization state. This proposal remains to be explored by in vitro and in vivo studies.

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Low-Molecular-Weight Heparin Versus Oral Anticoagulant Therapy for the Long-Term Treatment of Symptomatic Venous Thromboembolism: Is There Any Difference in Cancer-Related Mortality?

To the Editor: Patients affected by advanced cancer are likely to develop venous thromboembolism (VTE). Its onset can increase comorbidities, diminishing the patient's quality of life and often compromising the regular administration of chemotherapy. Patients with malignancy treated with oral anticoagulant therapy (OAT) have a higher